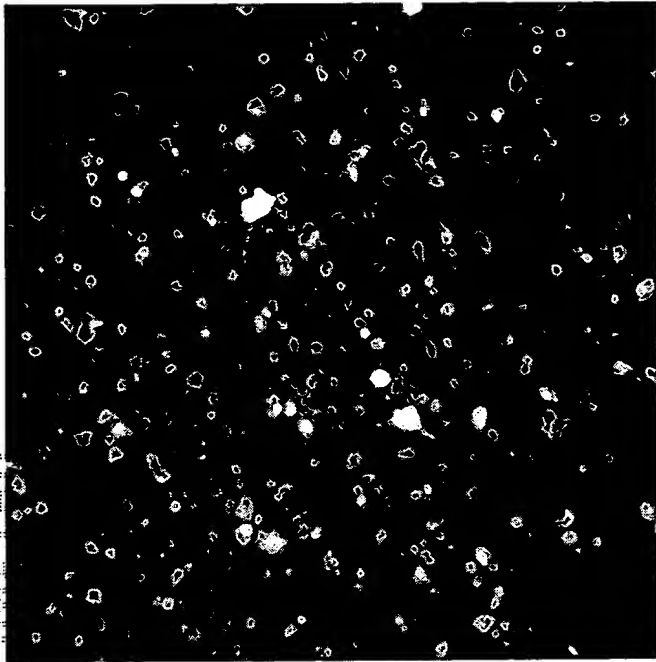
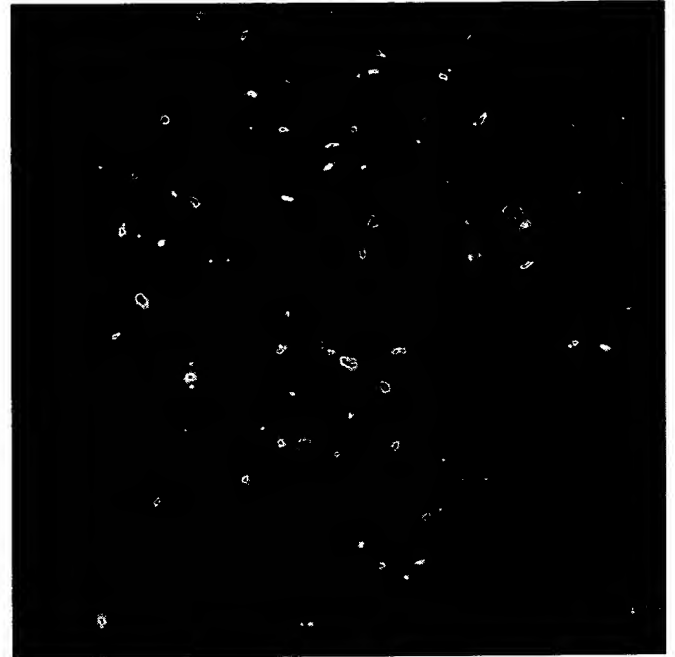


Figure 1

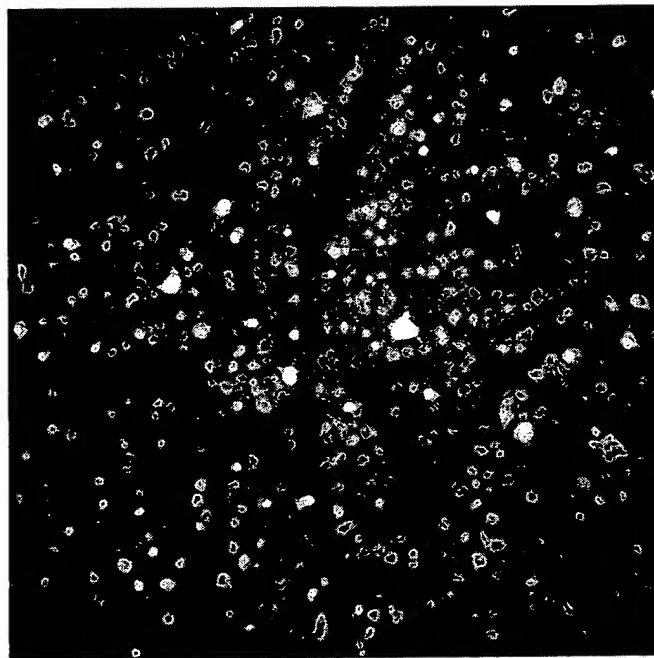
GPI 1046 protects ganglion cells against degeneration due to 1 hour of retinal ischemia  
Fluorogold labelled retinal ganglion cells in wholemount, 28 days after ischemic episode



A. Labelled retinal ganglion cells in the Normal central retina

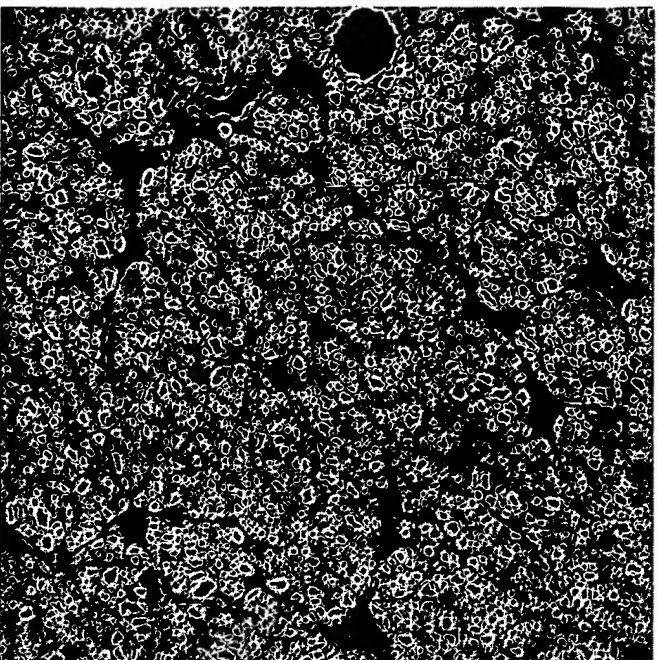


B. 1 hour of retinal ischemia produces extensive loss of ganglion cells

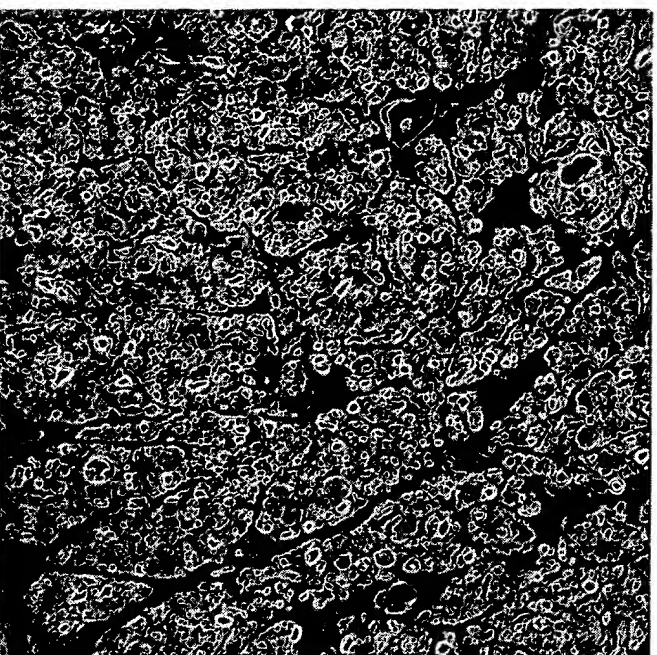


B. Administration of GPI 1046 1 hour before retinal ischemia and for 4 days subsequently produces significant protection of vulnerable retinal ganglion cells

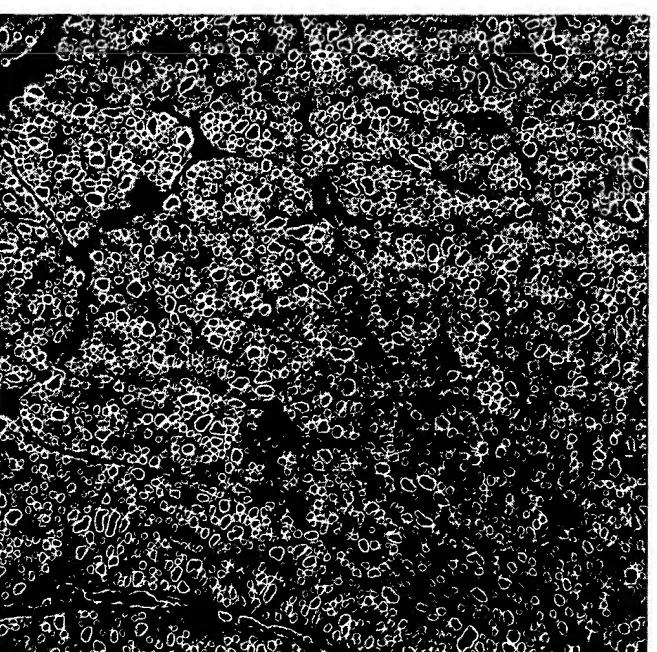
**Figure 2**  
**GPI 1046 Protects retinal ganglion cell axons and prevents myelin degeneration**  
**in the optic nerve induced by 1 hour of complete retinal ischemia,**  
**toluidine blue stained optic nerve cross sections, 630X**



**A. Normal optic nerve**

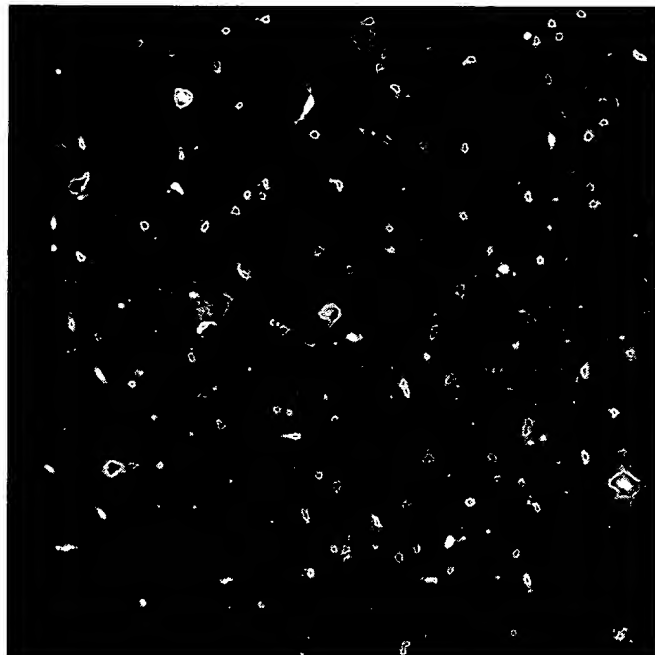


**B. Vehicle treated optic nerve 28 days**  
**after 1 hour complete retinal ischemia**



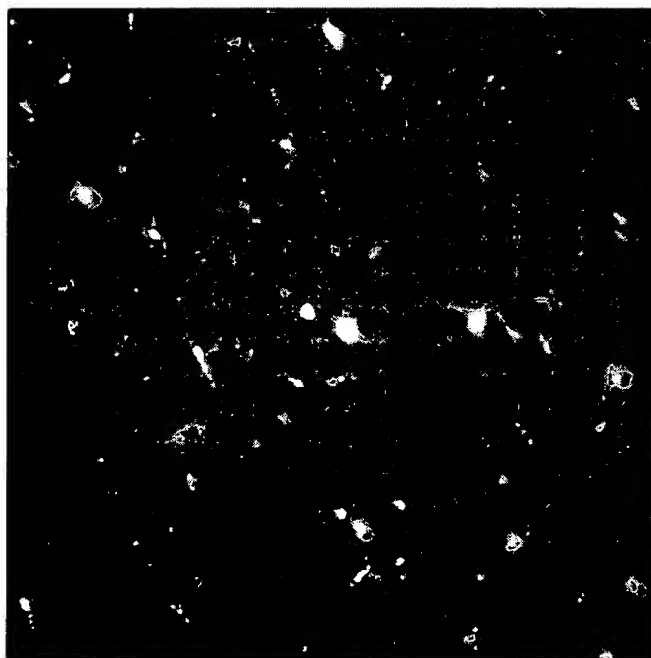
**C. GPI 1046 treated optic nerve 28 days**  
**after 1 hour complete retinal ischemia**

**GPI 1046 administration for 28 days  
provides only moderate protection of  
axotomized retinal ganglion cells**



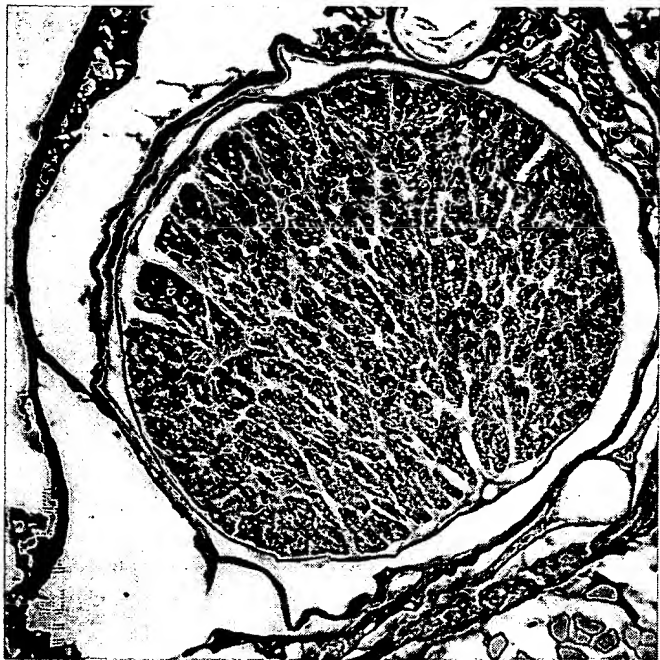
Fluorogold labelled RGCs 90 days following transection,  
Treatment with vehicle alone for 1<sup>st</sup> 28 days

Fluorogold labelled RGCs 90 days following transection,  
Treatment with GPI 1046 for 1<sup>st</sup> 28 days  
Treatment with vehicle alone for 1<sup>st</sup> 28 days



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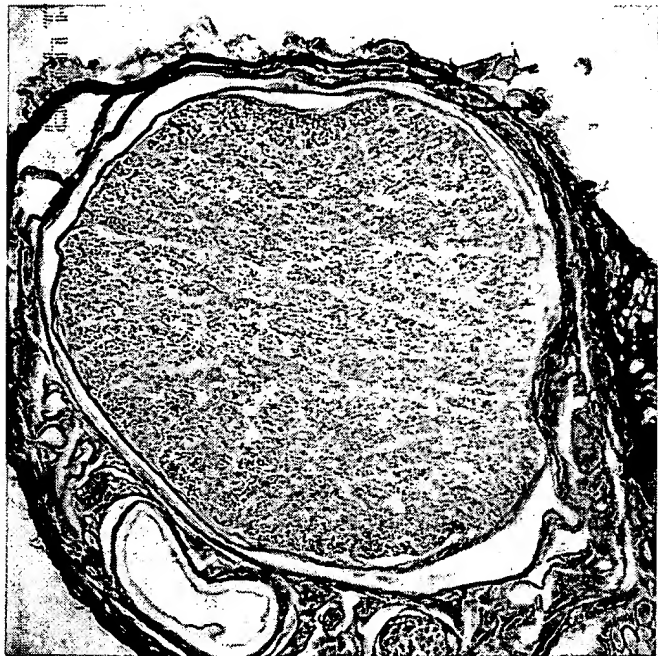
**Figure 4**  
**GPI 1046 prevents axonal degeneration in the proximal stump of the optic nerve**  
**RT97 neurofilament immunohistochemistry,**  
**optic nerve cross sections, 90 days after complete transection**



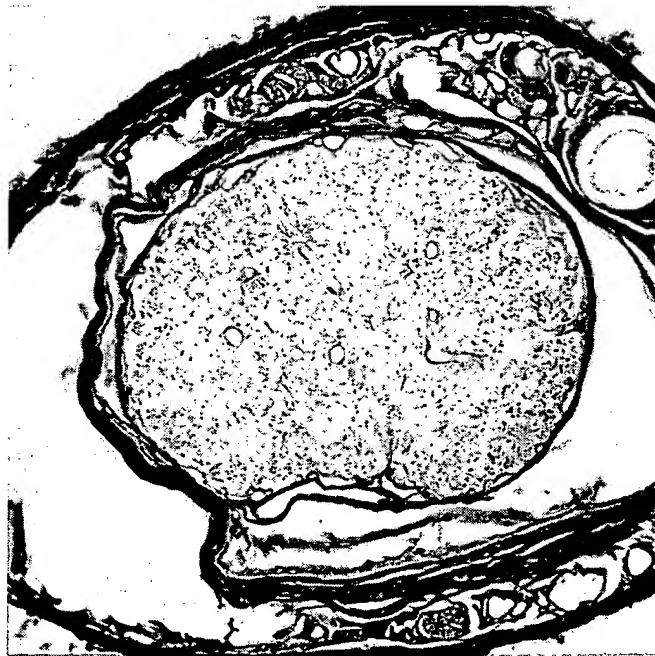
**A. Sham**



**B. Optic nerve transection (ONT) 90 days survival**



**C. optic nerve 90 days after transection,  
GPI 1046 treatment days 1-28**

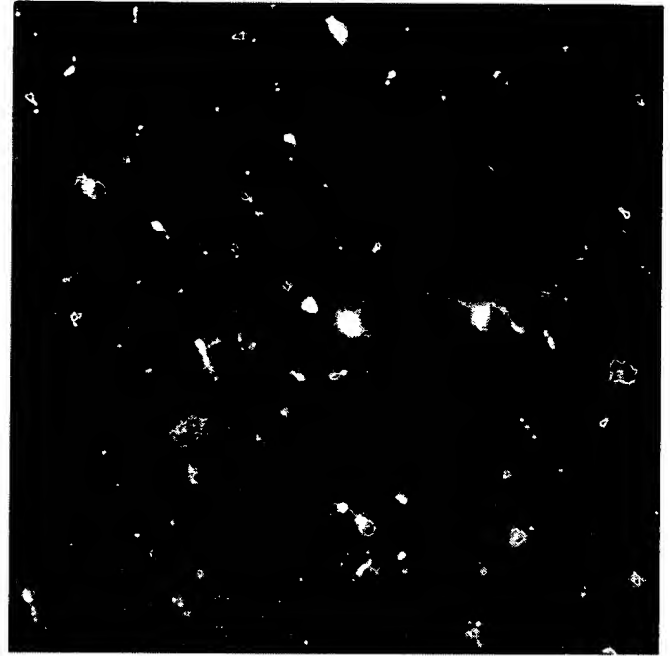


**D. optic nerve 90 days after transection,  
GPI 1046 treatment days 1-14**

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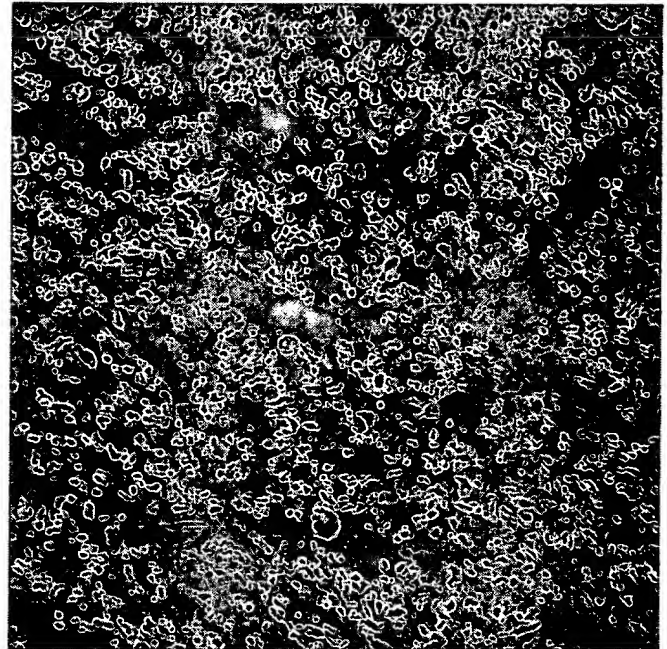
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**Fluorogold labelled retinal ganglion cells 90 days following transection**



### GPI 1046 administered for 1<sup>st</sup> 28 days

## RT 97 neurofilament immunohistochemistry 90days after transection



### GPI 1046 administered for 1<sup>st</sup> 28 days

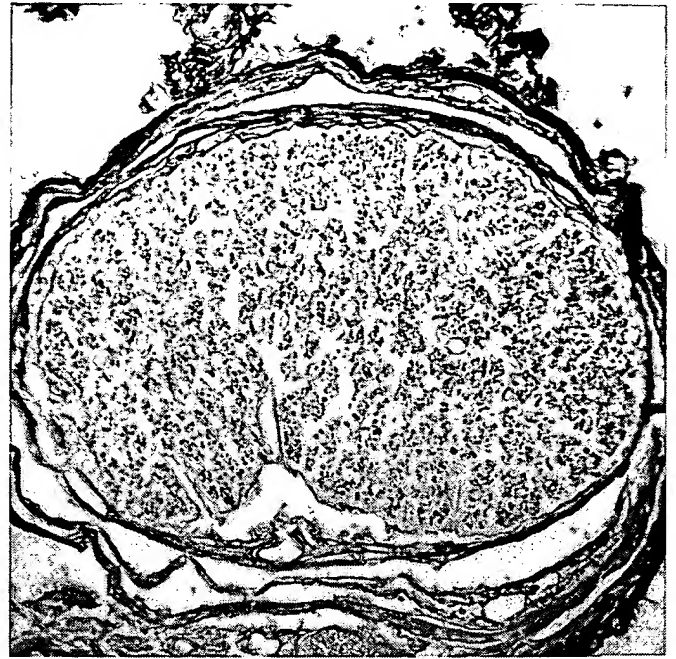


Figure 6

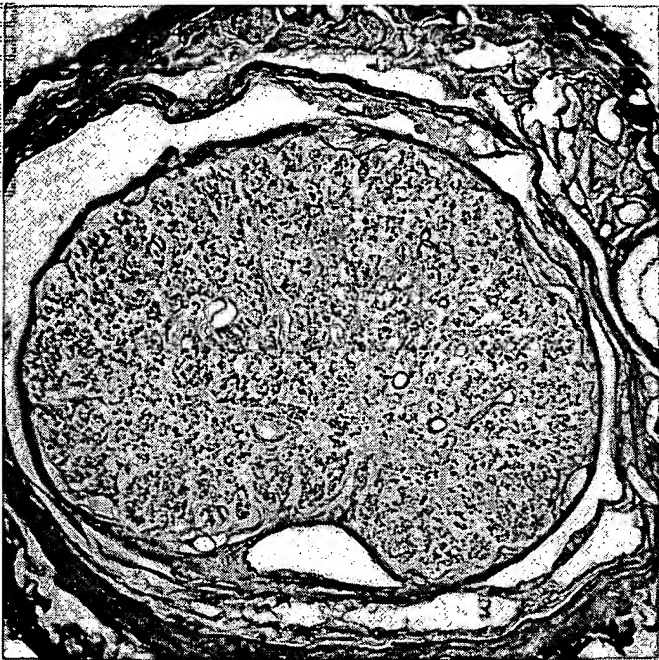
**Preservation of myelin in the proximal stump of the optic nerve 90 days after transection  
14 vs 28 days treatment with GPI 1046 10mg/kg s.c.**



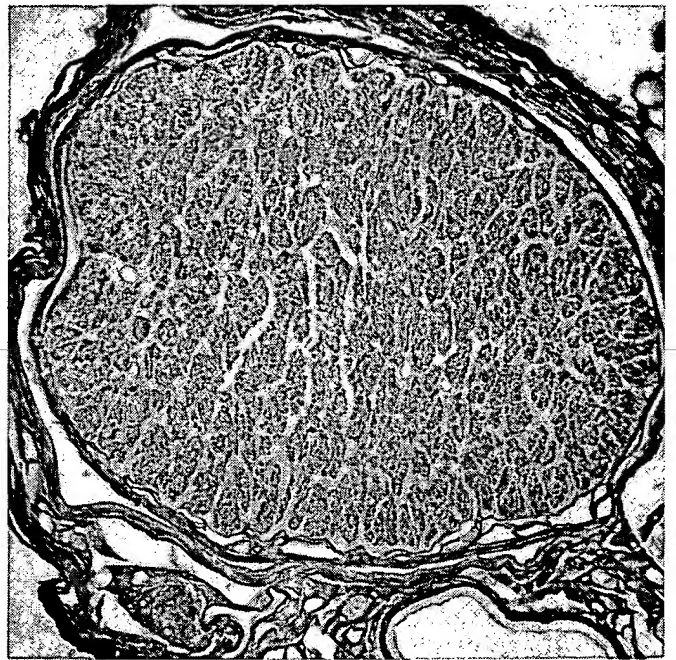
**Normal( sham) Optic nerve**



**90 days after optic nerve transection, vehicle treated**



**90 days after optic nerve transection, 14 days GPI 1046**



**90 days after optic nerve transection, 28 days GPI 1046**

**myelin basic protein immunohistochemistry (SMI-94), 20X**

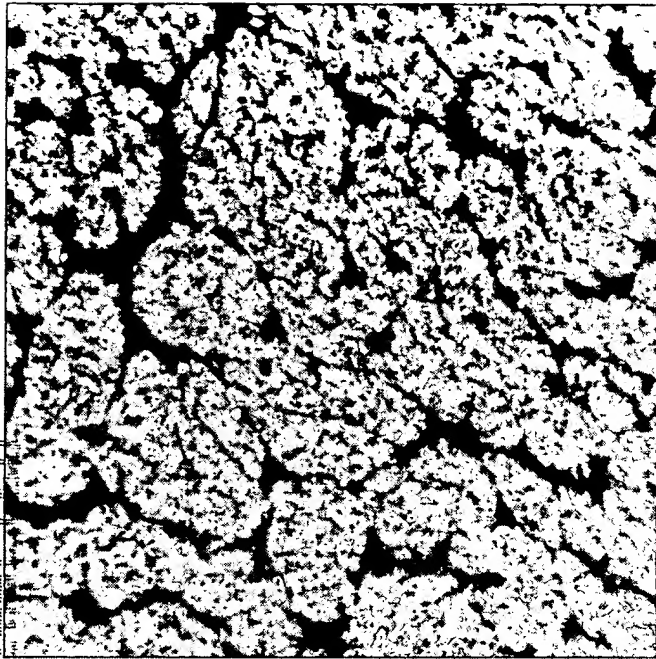
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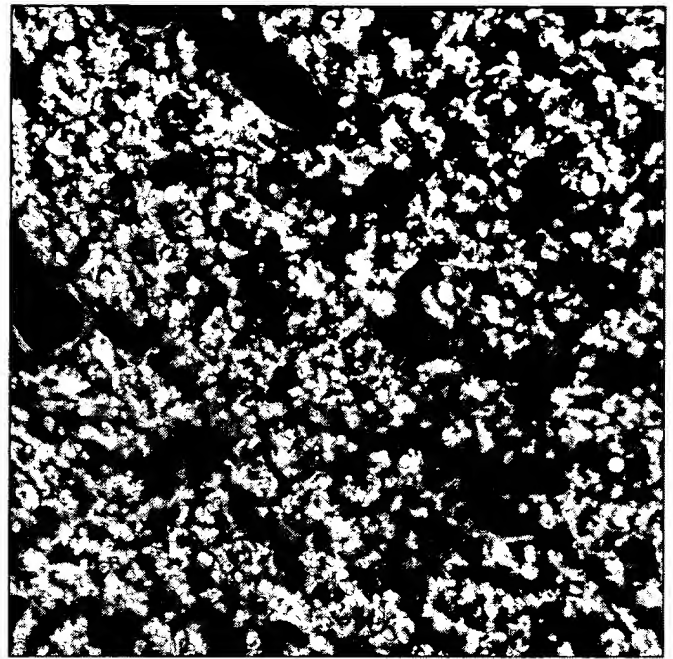
**Figure 7**  
**FKBP-12 immunohistochemistry labels oligodendroglia and axons in the normal optic nerve**

Figure 8

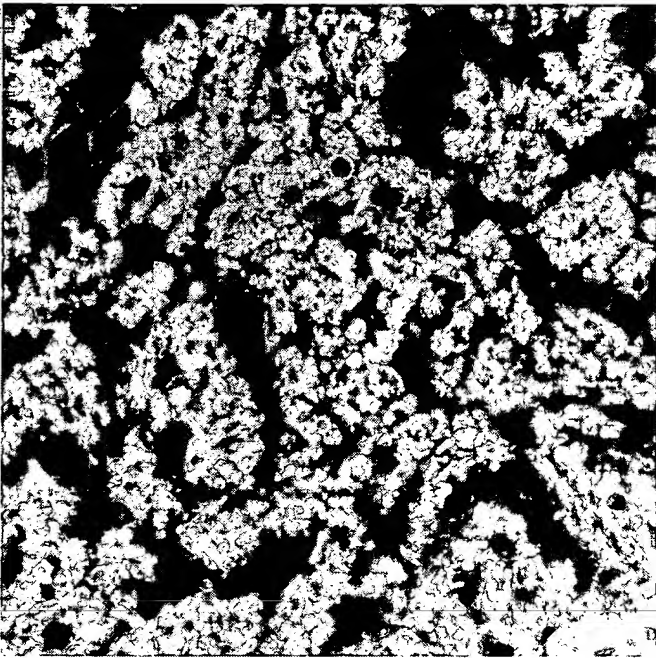
**GPI 1046 treatment prevents myelin degeneration  
in the distal stump of the optic nerve  
Myelin basic protein immunohistochemistry 90 days after transection**



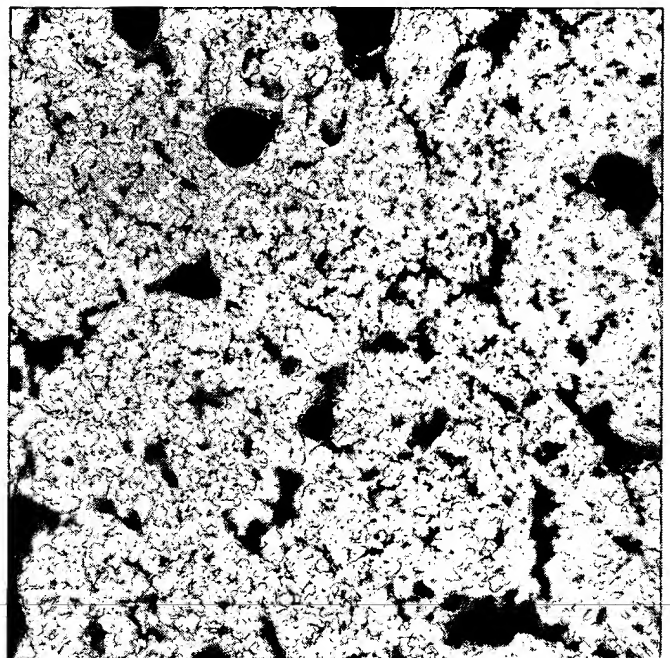
**A. Normal optic nerve**



**B. Distal optic nerve stump  
90 days after complete transection**



**C. Distal optic nerve stump  
90 days after complete transection  
GPI 1046 administered 1-14 days  
after transection**



**D. Distal optic nerve stump  
90 days after complete transection  
GPI 1046 administered 1-28 days  
after transection**



Figure 9

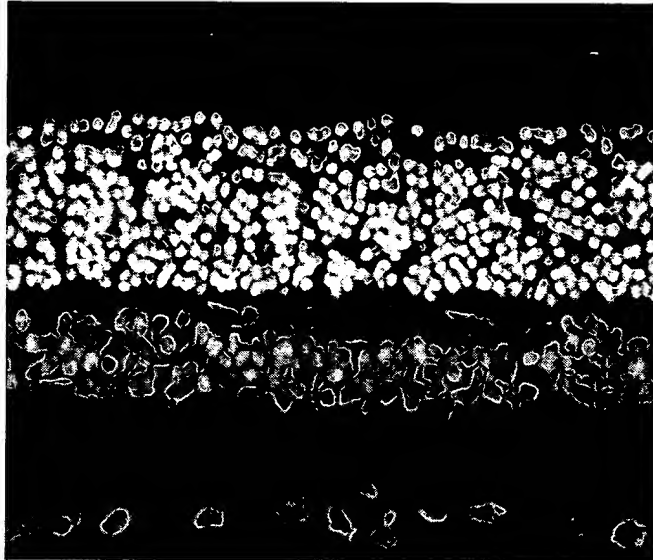
**GPI 1046 decreases neovascularization and prevents neuronal loss  
in the inner retina in the Streptozotocin model of diabetic retinopathy**

**A. Normal  
retina  
Cross section  
Cresyl violet**

**Outer Nuclear  
layer (ONL)**

**Inner Nuclear  
layer(INL)**

**Ganglion cell  
layer (GCL)**

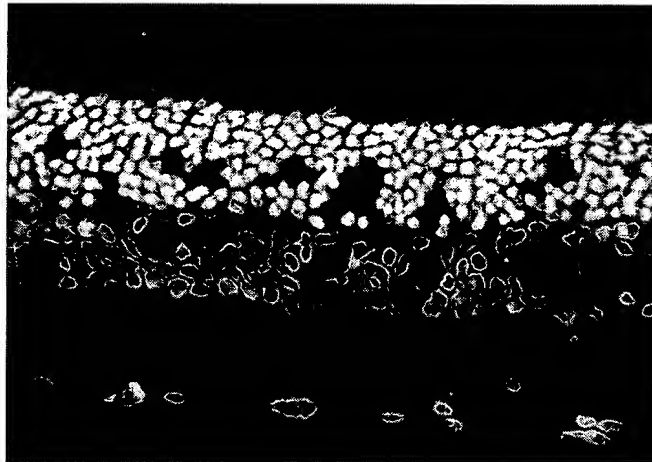


**B. retina from  
Streptozotocin  
/vehicle case**

**ONL**

**INL**

**GCL**

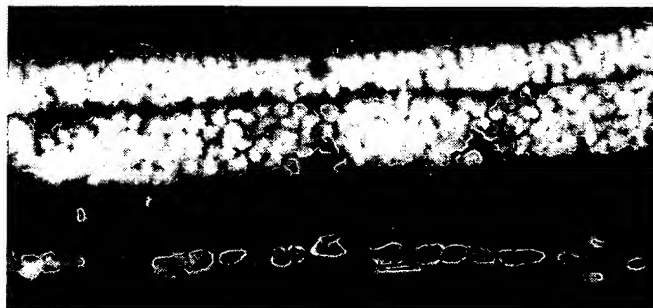


**C. Retina from  
Streptozotocin  
/GPI 1046 case**

**ONL**

**INL**

**GCL**



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